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FDAMA Section 113:

Information Program on Clinical Trials for Serious and Life-Threatening Diseases

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Background:

Section 113 of the 1997 Food and Drug Administration Modernization Act creates a public resource for information on studies conducted under FDA's investigational new drug (IND) regulations (21 CFR part 312) for drugs, including biological drug products, to treat serious or life-threatening diseases and conditions.

Section 113 directs the Secretary of Health and Human Services, acting through the director of NIH, to establish, maintain, and operate a data bank of information on clinical trials for drugs to treat serious or life-threatening diseases and conditions.

The Clinical Trials Data Bank must contain (1) information about federally and privately funded clinical trials for experimental treatments for patients with serious or life-threatening diseases, (2) a description of the purpose of each experimental drug, (3) patient eligibility criteria, (4) a description of the location of clinical trial sites, (5) a point of contact for patients wanting to enroll in the trial.

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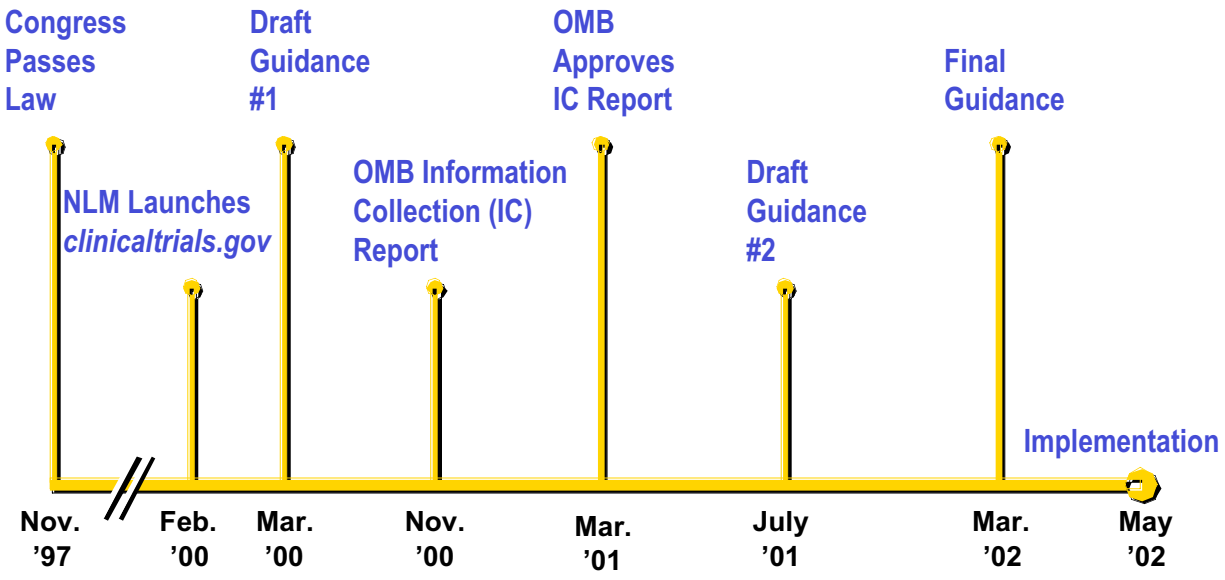
Implementation Timeline



Provides easy access to information on clinical trials for a wide range of diseases.

FDA prepared a report for its estimate of the annual reporting burden related to the extracting & reformatting of information for the database.

Sponsors were given 45 days after the final guidance document issued to list existing or ongoing trials.

Provided information on the types of clinical trials for which submissions are required.

Addressed procedural issues including how to submit protocol information via a web-based Protocol Registration System.

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What trials should be listed in ClinicalTrials.gov?

A clinical trial conducted under an IND is required to be submitted to *ClinicalTrials.gov* if it is a drug to treat a **serious or life-threatening** disease or condition AND it is a trial to test **effectiveness**.

Life-threatening is defined as:
(1) diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and (2) diseases or conditions with potentially fatal outcomes, where the endpoint of clinical trial analysis is survival.

The ***seriousness*** of a disease is based on factors such as survival, day-to-day functioning, and the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.

Phase 2, phase 3 and phase 4 trials with efficacy endpoints are trials to test effectiveness.

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Objectives:

» To educate non-NCI sponsors about statutory requirements under FDAMA Section 113, the final guidance document, and the availability of the web-based data entry tool, Protocol Registration System (PRS), developed by the National Library of Medicine, National Institutes of Health.

» To measure the number of **cancer** protocols made available through *ClinicalTrials.gov* and compare to the protocols submitted to the Center for Drug Evaluation and Research (CDER) between January 1 and September 30, 2002.

» To evaluate sponsor participation in *ClinicalTrials.gov.*

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Methods:

» New cancer protocols submitted to CDER between January 1 and September 30, 2002 (n = 366) were identified from a search of the COMIS database, a management information system in CDER.

» Letters were mailed to non-NCI sponsors informing them of the guidance document and how to submit trial information using the PRS.

» Protocol information (indication, protocol title, phase, sample size, location and efficacy endpoints) was abstracted and entered in a Microsoft Access database. In addition to the COMIS indication, a revised indication, using NLM's Medical Subject Headings (MeSH), was also entered into the database.

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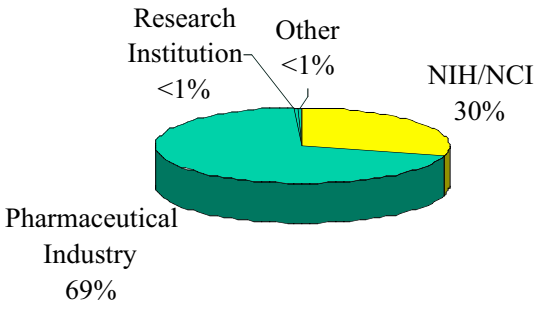
Results:

» 366 ***cancer*** protocols were submitted to CDER between January 1 and September 30, 2002:

- 255 (69%) pharmaceutical industry protocols
- 108 (30%) NIH/NCI protocols
- 3 (<1%) research institution and other protocols



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Cancer Protocols Submitted to CDER by Phase (n = 366)

	1	1/2	2	2/3	3	4	NS
NIH/NCI (n = 108)	35	10	54	0	4	0	5
Pharmaceutical Industry (n = 255)	103	14	89	7	34	4	4
Research Institution (n = 1)	0	0	1	0	0	0	0
Other (n = 2)	0	0	0	0	2	0	0
TOTAL:	**138 (38%)**	**24 (7%)**	**144 (39%)**	**7 (2%)**	**40 (11%)**	**4 (1%)**	**9 (2%)**

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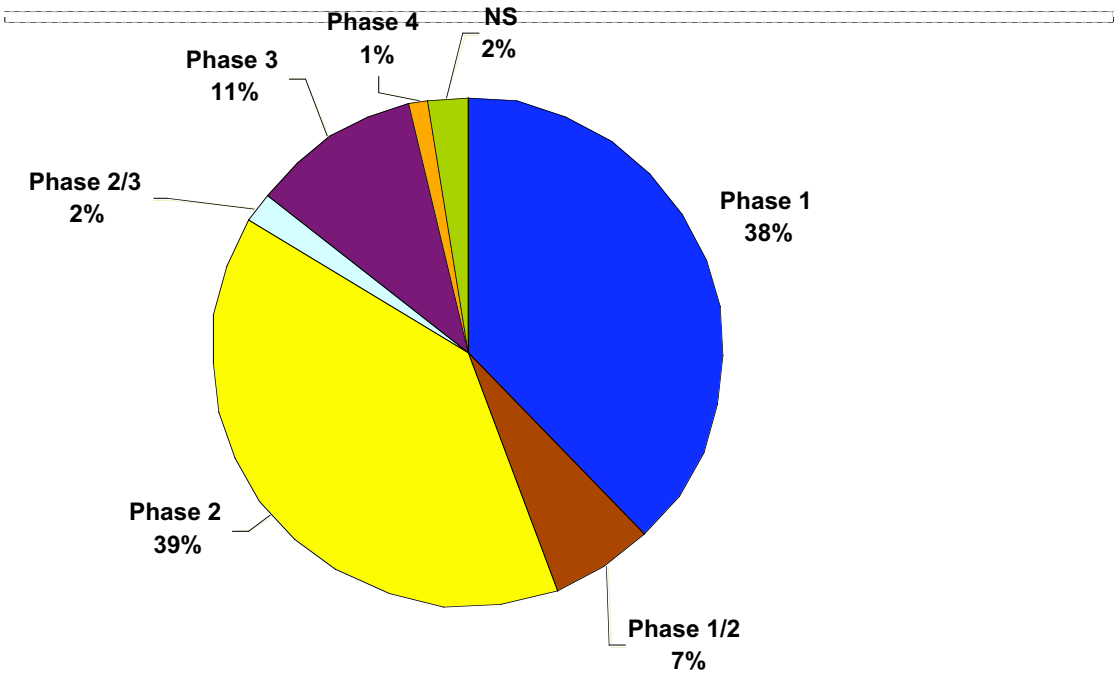

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» 187 out of 366 (51%) CDER cancer protocols met the criteria for listing in *ClinicalTrials.gov*.

» Of those 187 protocols:
- 127 (68%) Pharmaceutical industry
- 57 (30%) NIH/NCI
- 1 (1%) Research institution
- 2 (1%) Other

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115 of the 187 (61%) cancer protocols have been submitted to *ClinicalTrials.gov*

» Pharmaceutical industry:
  - 61 out of 127 (48%) protocols

» NIH/NCI:
  - 52 out of 57 (91%) protocols

» Research institution:
  - 0 out of 1 (0%) protocol

» Other:
  - 2 out of 2 (100%) protocols

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	Pharmaceutical Industry (n = 255)	NIH/NCI (n = 108)	Research Institution (n = 1)	Other (n = 2)
% Participation	48%	91%	0%	100%

**Based on data collected from January 1 - September 30, 2002*

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Discussion:

» The 115 cancer protocols submitted to *ClinicalTrials.gov* are specifically from the time frame of the educational program and only include protocols submitted to CDER. Additional protocols are listed in *ClinicalTrials.gov* and may have been submitted voluntarily, outside the time frame of the program, or were CBER protocols.

» Sponsors were not required to submit their existing and ongoing protocols until the May 2, 2002 implementation date. Pharmaceutical industry participation from January 1 - May 1, 2002 (pre-implementation date) was 49%. The participation rate after the May 2 implementation date was 46%.

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- Based on discussions with some representatives from the pharmaceutical industry, in some instances protocols that met the requirement for listing were not submitted due to lack of funding for the study or the initial enrollment date was delayed.

- For the 5 NIH/NCI protocols not listed, specific reasons were not identified as part of the study. It is reasonable to assume the protocols were not listed due to funding issues or delayed enrollment.

- Monitoring of protocol listings in *ClinicalTrials.gov* continued through April 1, 2003. It was expected that the pharmaceutical industry participation rate would have been higher than 46%.

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Conclusion:

Participation by the pharmaceutical industry was less than expected one year after the availability of a final guidance document despite a federal law, a targeted educational program, and an easy-to-use web-based data entry tool.

Additional analyses are necessary to elucidate other factors that may impact a company's decision to list a cancer clinical trial in the ClinicalTrials.gov data bank.